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ZOÖLOGY ANATOMY PHYSIOLOGY NEUROLOGY BOTANY PATHOLOGY BACTERIOLOGY

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THE LECITHANS

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THEIR FUNCTION IN THE LIFE OF THE CELL

WALDEMAR KOCH

THE ash left on the incineration of tissues obtained from various parts of the body, especially the brain, has long been known to contain phosphorus. Of the chemical combination in which this phosphorus was present in the original tissues nothing was known until Gobley[1] carefully studied an organic phosphorus-containing body, which he isolated from eggs and called lecithin. He obtained as splitting products glycerophosphoric acid and some of the fatty acids. Diaconow[2] continued this work at the suggestion of Hoppe Seyler, and isolated as splitting products glycerophosphoric acid, stearic and oleic acids, and a base which he identified with Baeyer's neurin and the neurin obtained by Liebreich[3] from his protagon by decomposition with barium hydrate. From the ease with which his lecithin could be split up Diaconow concluded that it was a neurin salt of distearyl glycerophosphoric acid. This view was, however, disproved by Hundeshagen[4] on account of the fact that the body prepared by the union of neurin and distearyl glycerophosphoric acid in alcohol solution would not give the characteristic myelin forms, although it possessed all the other properties of lecithin. Strecker[5] brought confusion into this subject by identifying the base obtained by him from lecithin with the cholin he had isolated from bile.[6] Thudichum[7] pointed out the difference between the body derived from bile and the base isolated from lecithin, and identified the latter as neurin by a number of analyses made with carefully purified material. In the book above referred to Thudichum also records some other important observations. Among the large number of compounds isolated by him from the brain there are some which do not contain glycerin; as he always finds phosphorus in the form of orthophosphoric acid, he concludes to call these bodies "Phosphatids" and consider them rather as derivatives of orthophosphoric acid than glycerophosphoric acid, as previously accepted. His formulæ resemble the types of the *Typentheorie* of Gerhardt and Wurtz, in leaving the exact building up of the molecule a matter of doubt. From a study of the fatty acids in his various compounds Thudichum concludes, contrary to Diaconow, that there are no phosphatids with only one fatty acid, but that each one contains either palmitic, stearic, or mar-

[1] GOBLEY, *Journal de pharmacie et de chimie* (1850), Vol. XVII, p. 401, and Vol. XVIII, p. 107.

[2] DIACONOW, *Hoppe Seylers medicinisch-chemische Untersuchungen*, 1866, Vol. II, p. 221; also *Centralblatt für die medicinischen Wissenschaften* (1868), Vol. VI, pp. 2, 97, and 434.

[3] LIEBREICH, *Liebig's Annalen der Chemie und Pharmacie* (1865), Vol. CXXXIV, p. 34.

[4] HUNDESHAGEN, *Journal für praktische Chemie* (1883), Vol. XXVIII, p. 219.

[5] STRECKER, *Liebig's Annalen der Chemie und Pharmacie* (1868), CXLVIII, p. 78.

[6] *Ibid.* (1862), Vol. CXXIII, p. 353.

[7] THUDICHUM, *Die chemische Konstitution des Gehirns des Menschen und der Tiere*, 1901, p. 123.

gearic as one of the constituents; which, however, gives no character to the molecule, while the other acid — oleic for brain lecithin, kephalinic for kephalin — gives to the molecule its distinctive properties.

Without considering further the important question of the structure of these compounds, I would propose to classify them under the general term "Lecithans." The introduction of the word "lecithan" as a group name seems preferable to the use of an entirely new and unfamiliar term like "phosphatids," as proposed by Thudichum. At the same time, the change of the last syllable of lecithin to *an* gives sufficient variation to prevent any such confusion as attended the generalization of the word "albumen." The lecithans, then, are substances containing in the molecule phosphoric acid, fatty acids, nitrogen, and, in most cases, glycerin. They resemble each other very closely in their physical appearance, being waxy, non-crystalline, and very hygroscopic. Toward water they all show the same behavior, although their solubility or the solubility of their salts in *organic* solvents may vary.

The very general distribution of the lecithans in all forms of living tissues speaks for their value in the life of the cell. A more careful study of these compounds indicates that they are valuable in two ways: first, on account of their physical properties; and, secondly, on account of their chemical behavior.

PHYSICAL PROPERTIES

The behavior of the lecithans with water seems of especial interest, and can be watched under the microscope. A waxy piece of brain lecithin placed in water first swells up and then gives off long filaments (called myelins) which sometimes resemble a shepherd's crook, at other times a mass of twisted skein. If allowed to stand for some time, with frequent shaking, a perfect emulsion is finally formed. A lecithan which has been part of the living tissues, such as brain lecithin, gives a much more perfect emulsion than egg lecithin, which is merely stored food material. If such an emulsion is the substratum of the living cell—and there seems good reason to consider it so—it may explain some of the physical properties of living protoplasm. The study of this emulsion is especially interesting in connection with the changes in the physical conditions of the living cell brought about by electrolytes, as shown by the recent work of J. Loeb and his school.

Action of electrolytes on an emulsion of brain lecithin.—Four g. of brain lecithin (free from calcium, and containing less than 1 per cent. sodium or potassium) are treated with one liter distilled water. The resulting emulsion is sufficiently transparent for purposes of study, can be filtered unchanged, has a neutral reaction to litmus, and remains unaltered for weeks, especially after sterilization by boiling. The results of my experiments with this emulsion may be classified as follows:

Univalent kations.— Salts of Na, K, NH_4, Li, Ag, even in very concentrated solution, give no precipitate and have apparently no effect on the emulsion. The hydrogen ion is an exception, in the case of acids which are sufficiently dissociated. A

concentration of $\frac{m}{200}$ sulphuric will give a precipitate. Carbonic acid is not sufficiently soluble to give any precipitate.

Divalent kations.—Mg, Ca, Sr, Ba, Co, Ni, Fe'', Zn, Cd, Cu, and Pb all give a precipitate which, similar to the one with acids, is flocculent, gelatinous, and settles to the bottom in less than one hour, leaving the supernatant liquid perfectly clear. The concentrations which will just give the precipitate vary somewhat and have been found in the case of Ca, Sr, and Ba to be $\frac{m}{100}$, $\frac{m}{40}$, and $\frac{m}{30}$, respectively.

Trivalent kations.— Fe''', Al, Au give no precipitate and behave like monovalent kations. Cr gives unsatisfactory results. Au, after standing for several hours, is precipitated in the metallic state.

Anions.— Cl, Br, I, SO_4'', *oxalate*, *citrate*, and *ferrocyanide* ($K_4Fe(CN)_6$) give no precipitate, and even in concentrated solution have no apparent effect on the emulsion. OH is an exception, causing the emulsion to clear up.

Non-electrolytes.—Albumins, peptones, glucose, urea, alkaloids, and narcotics like urethan and chloral give no precipitation reactions and leave the emulsion apparently unchanged. Chloroform has a tendency to be emulsified by the emulsion, a reaction which Thudichum had already observed with ether.

The precipitations above observed with the hydrogen ion and divalent kations seem to be of an entirely physical nature because:

1. They are independent of the concentration of the lecithin. An $\frac{m}{2000}$ lecithin emulsion will begin to precipitate with about the same concentration of the divalent kation as an $\frac{m}{200}$ emulsion. Stronger emulsions are not sufficiently transparent for observation.

2. Removal of the supernatant liquid by decantation and the addition of water will cause the precipitates to redissolve.

Cadmium, copper, and other salts of various lecithans have been prepared in alcohol solution and analyzed, but they are readily broken up on the addition of water, and belong to a class of physical compounds even more unstable than ordinary double salts. It would seem, then, that when a certain limiting concentration of the divalent kation is reached, the emulsion can no longer exist and the lecithin is precipitated, carrying with it possibly some of the salt. Very interesting, on account of the possibility of furnishing an explanation of such results as Loeb[8] obtains with Fundulus, are the antagonistic effects of univalent kations in preventing the precipitation. Near the limits at which Ca will just give a precipitate, a very small amount of Na will suffice to prevent this precipitate; as more Ca is added, relatively more Na is needed. A direct comparison of my results with J. Loeb's is not possible, because, in the first plece, the amounts of Ca, Na, and lecithin in the Fundulus egg are not known, and, in the second place, the reaction between the solution and the egg does not come about as

[8] LOEB, *American Journal of Physiology* (1902), Vol. VI, p. 411.

directly as in my case. The following table gives the data obtained with an emulsion of brain lecithin:

			After Three Hours
I.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. water	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ - - Immediate ppt.	Ppt. settled
II.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. 5 m NaCl	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ - - No ppt.	No ppt.
III.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. $\frac{m}{10}$ NaCl	+ 1.5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ - - No ppt.	No ppt.
IV.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. $\frac{m}{10}$ NaCl	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ - - Immediate ppt.	Ppt. settled
V.	5 c.c. $\frac{m}{200}$ emul. + 5 c c. $\frac{m}{10}$ NaCl	+ 3.5 c.c. $\frac{m}{10}$ $Sr(NO_3)_2$ - - No ppt.	No ppt.
VI.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. $2\frac{1}{2}$ m KCl	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ - - No ppt.	No ppt.
VII.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. $\frac{m}{10}$ $FeCl_3$	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ - - No ppt.	No ppt.
VIII.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. urea concentrated solution	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ Ppt. formed slowly	Ppt. settled
IX.	5 c.c. $\frac{m}{200}$ emul. + 5 c.c. glucose concentrated solution	+ 5 c.c. $\frac{m}{10}$ $Ca(NO_3)_2$ Ppt. formed slowly	Ppt. settled

We may conclude, then, that the precipitation of lecithin by divalent kations is a physical phenomenon probably of an electrical nature, because:

1. Non-electrolytes do not prevent the precipitation (I, VIII, IX).

2. The trivalent kation Fe''' is much more efficient in preventing the precipitation than a monovalent one like Na (II, VII).

3. The precipitate is formed independent of the concentration of the lecithin and can be redissolved by the addition of water.

The application of these observations to Loeb's results must be postponed until other lecithans have been more carefully studied.

CHEMICAL PROPERTIES

The chemical properties of the lecithans depend on two groups in the molecule: first, the fatty acids, and, second, the complex of which the nitrogen is a part. The phosphoric acid, although the nucleus and very important in the building up of the molecule, does not seem to enter into any reaction, except on the complete destruction of the lecithan; as Halliburton[9] has found the phosphorus to decrease in degenerating nerves only after the eighth day.

Each lecithan contains, according to Thudichum, two fatty acids in the molecule: one—either palmitic, stearic, or margaric—does not impart any particular property to the compound; the other—oleic in the case of lecithin, kephalinic in the case of kephalin—gives to the molecule its distinctive character. This distinctive group is always unsaturated, will therefore add iodine, and bring about the reduction of osmic acid. Upon this group, then, depends the use of osmic acid as a stain for nervous

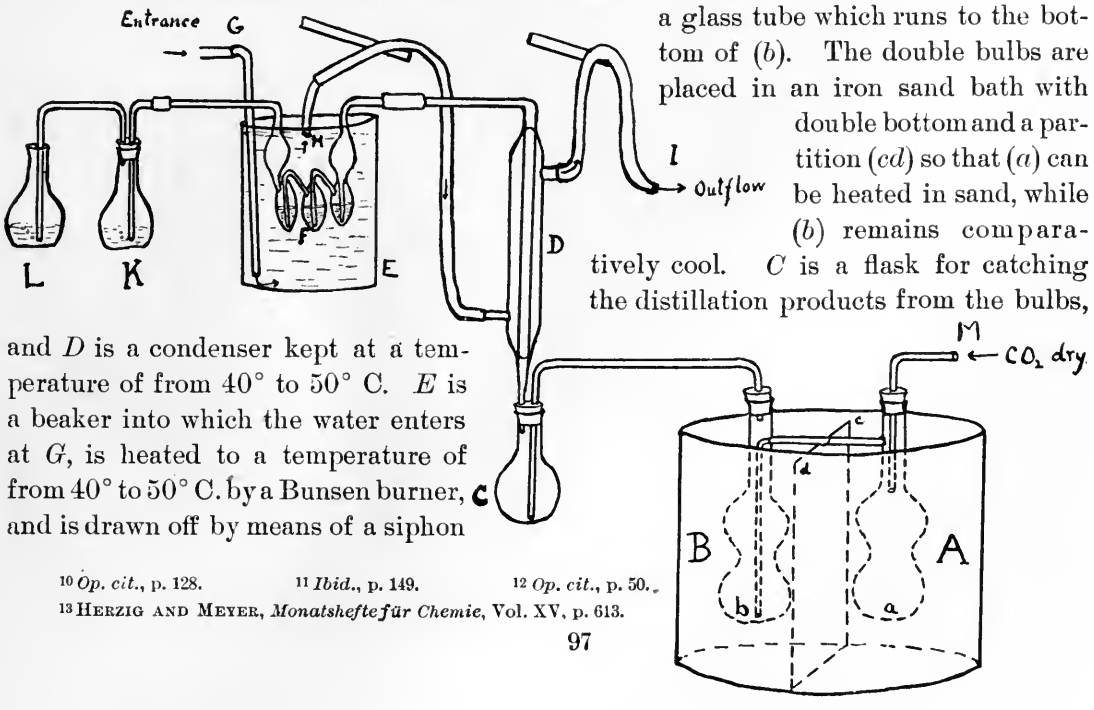
[9] W. D. HALLIBURTON, *The Chemical Side of Nervous Activity*, 1901, p. 87.

tissues in histological technique. The value of osmic acid as a general test for fats depends on the fact that all fats in the body contain some oleates. Pure stearates and palmitates will not give the test. The darkening of the lecithans on exposure to the air is also dependent on this group. In the case of kephalin, the change on exposure to the air takes place so rapidly as to suggest an autoxidizable substance capable of activating oxygen. The guiac-blue reaction, however, gives a negative result; and Thudichum[10] has shown that kephalin exposed to an atmosphere of oxygen in a eudiometer will not decrease the volume of the gas. The change is probably due to an internal rearrangement in the molecule, and takes place within the molecule of the fatty acid itself; as Thudichum[11] obtained from kephalin an acid by saponification (kephalinic acid) which exhibited the same changes as the mother-substance.

Less apparent, but nevertheless important, are the changes which the molecules of the lecithans undergo in the complex which contains the nitrogen. Thus Halliburton[12] has found the cholin to increase in the cerebro-spinal fluid as the result of general paralysis. For the quantitative investigation of the cholin or neurin the methyl groups attached to the nitrogen seem especially useful, as Herzig and Meyer[13] have devised a method by which such groups can be accurately determined. The description of the method is not easily accessible. I will therefore repeat it here, with such modifications as have been found useful, before going on to describe the results obtained with lecithans from various sources.

HERZIG AND MEYER'S DETERMINATION OF METHYL ATTACHED TO NITROGEN

The apparatus consists of a double glass bulb, 4 cm. wide at the largest diameter and 2½ cm. at the narrowest diameter, and 12 cm. high. The bulb (*a*) is connected to (*b*) by a glass tube which runs to the bottom of (*b*). The double bulbs are placed in an iron sand bath with double bottom and a partition (*cd*) so that (*a*) can be heated in sand, while (*b*) remains comparatively cool. *C* is a flask for catching the distillation products from the bulbs, and *D* is a condenser kept at a temperature of from 40° to 50° C. *E* is a beaker into which the water enters at *G*, is heated to a temperature of from 40° to 50° C. by a Bunsen burner, and is drawn off by means of a siphon



[10] *Op. cit.*, p. 128. [11] *Ibid.*, p. 149. [12] *Op. cit.*, p. 50.
[13] HERZIG AND MEYER, *Monatshefte für Chemie*, Vol. XV, p. 613.

at *H*, to enter the condenser *D* and keep it at the proper temperature. By regulating the flow of the water and the height of the flame, the temperature of the water can easily be kept within the required limits. *F* are Geissler bulbs for absorbing everything but the methyl iodide, which is absorbed in *K* and *L*. The analysis is carried on as follows: 0.2 g. of the substance to be analyzed is placed in (*a*) with 2 g. of dry ammoniun iodide and enough hydriodic acid (sp. gr. 1.6) to half fill the lower bulb. In (*b*) is placed 1 g. of ammonium iodide. The part *A* of the sand bath is filled with sand and a thermometer reading to 360° C. placed in the sand. A stream of dry CO_2 is allowed to enter at *M*, and when all the air is displaced, a triple burner is lighted under the sand bath. In the meanwhile the water must be started and kept running through the condenser *D* at a temperature of from 40° to 50° C. As the temperature of 200° C. is reached in the sand bath, methyl iodide begins to split off and is carried over by the CO_2 mixed with hydriodic acid and iodine. Most of the iodine and hydriodic acid is condensed at *D* and collected in *C*. Some passes over and is absorbed in *F*, which contains the following solution:

Sodium carbonate - - - - -	1 part
Potassium arsenite - - - - -	1 part
Water - - - - - - - -	10 parts

The methyl iodide passes on and is collected in *K*, which contains 2 g. of silver nitrate dissolved in 5 c.c. water and 45 c.c. absolute alcohol. The methyl iodide dissolves in the alcohol, and is decomposed by the silver nitrate with the formation of silver iodide. After some time the temperature in the sand bath gradually rises to 240° C., and after a little while longer methyl iodide ceases to come over, as can be seen by the liquid in *K* becoming perfectly clear. *L*, which also contains silver nitrate, is used merely as a guard. The solution can be removed at this point, and the silver iodide collected corresponds to all the kephalin and one methyl group of the lecithin. Fresh silver nitrate is placed in *K*, another burner placed under the sand bath, and the temperature raised to 300° C. The remaining two methyl groups of lecithin come over, while kephalin gives off no more, or only a trace, of methyl iodide. The second part of the sand bath, *B*, is now filled with sand and heated to 300° to decompose anything which may have escaped previous heating. The two alcoholic solutions containing the silver iodide are diluted with much water and warmed for several hours on a steam bath to remove alcohol. Strong nitric acid is then added, and the silver iodide filtered into a Gooch crucible and weighed. In case we are not dealing with a mixture of lecithans, all the silver iodide can be weighed in one portion.

PREPARATION AND ANALYSES OF VARIOUS LECITHANS

Egg lecithin.—The yolks of ten eggs are allowed to stand with 600 c.c. ether over night, 1 liter alcohol added, the solution filtered and evaporated on water bath. The residue is dissolved in 200 c.c. cold ether and 1 liter acetone added. The precipitated

lecithin is treated over night with 1 liter cold alcohol, the solution filtered and evaporated. The residue is once more dissolved in ether, precipitated with acetone, and dried over sulphuric acid in a vaccuum desiccator.

I.[14] 0.8113 g. of the substance gave 0.1136 g. $Mg_2P_2O_7$; *i. e.*, 3.91 per cent. P.

II. 0.9150 g. of the substance gave 0.1278 g. $Mg_2P_2O_7$; *i. e.*, 3.90 per cent. P.

III. 0.330 g. of the substance gave 0.3001 g. AgI; *i. e.*, 5.80 per cent. CH_3.

IV. 0.325 g. of the substance gave 0.2960 g. AgI; *i. e.*, 5.81 per cent. CH_3.

V. 0.320 g. of the substance gave, below 240° C., 0.0760 g. AgI; *i. e.*, 153 per cent. CH_3. The methyl iodide given off above that temperature was lost on account of an accident. In III and IV the methyl iodide came over at 220° C. and 300° C. The two portions were not separated.

Phosphorus as 3.97 calculated for		Found		
		III	IV	V
3 CH_3:	5.66	5.80	5.81	
1 CH_3:	1.88			1.53

Brain lecithin and kephalin.—One kilo sheep's brains is minced in a meat-chopper and freed from water and extractives by boiling with 1 kilo acetone for eight hours. The solution is filtered cold, and the remaining acetone removed from the brains by gentle heating at 50° C. Seven hundred c.c. cold ether are now added and allowed to stand for three days, the solution is filtered, and another portion of ether added, and again allowed to stand. The ether filtrates are united and slowly evaporated to one-fourth their original volume in a tall beaker. The solution is then carefully removed by means of a pipette from the white precipitate, which has settled to the bottom, and 1.5 kilo alcohol is added to the solution.

Kephalin.—The precipitated kephalin is extracted five times with boiling alcohol, dissolved in ether, precipitated with acetone, again dissolved in ether, and allowed to settle in a long, narrow, closed test-tube. The clear ether solution is removed by decantation, evaporated, and the residue recrystallized twice from hot acetic ether. The resulting kephalin is very hygroscopic and must be dried over sulphuric acid for analysis. It agrees perfectly in all its properties with the kephalin described by Thudichum (p. 127). On analysis it gave the following results:

I. 0.2469 g. of the substance gave 0.5388 g. CO_2 and 0.2159 g. H_2O; *i. e.*, 59.5 per cent. C and 9.7 per cent. H.

II. 0.415 g. of the substance neutralized 5.2 c.c. $\frac{n}{10}$ acid; *i. e.*, 1.78 per cent. N.

III 0.9644 g. of the substance gave 0.1330 g. $Mg_2P_2O_7$; *i. e.*, 3.85 per cent. P.

IV. 0.7235 g. of the substance gave 0.0990 g. $Mg_2P_2O_7$; *i. e.*, 3.82 per cent. P.

V. 0.3488 g. of the substance gave, below 240° C., 0.0945 g. AgI; *i. e.*, 1.73 per cent. CH_3.

VI. 0.490 g. of the substance gave, below 240° C., 0.1312 g. AgI; *i. e.*, 1.71 per cent. CH_3.

[14] For phosphorus determinations the very excellent method of Neumann was used (*Engelmann's Archiv für Physiologie*, 1900, p. 159).

VII. 0.225 g. of the substance gave, below 300° C., 0.0636 g. AgI; *i. e.*, 1.80 per cent. CH_3.

VIII. 0.748 g. of the substance were burned with a mixture of nitric and sulphuric acid, the solution diluted, neutralized with 50 g. barium hydrate to remove sulphates and phosphates, the barium removed with sulphuric acid, and the solution evaporated. The ignited residue weighed 0.030 g. Some of this must have come as an impurity from the barium hydrate. In any case, the amount is not sufficient to account for any more than an impurity. Thudichum[15] has also found his kephalin to contain small amounts of inorganic substances as impurities. My analyses agree fairly well with Thudichum's (p. 132):

Thudichum: C, 60.0; H, 9.38; N, 1.68; P, 4.27
My results: C, 59.5; H, 9.7; N, 1.78; P, 3.84

The methyl groups correspond very closely to one methyl for one nitrogen. That this is not due to the presence of lecithin as an impurity is shown by the fact that the methyl is all split off below 240° C.

Phosphorus as 3.83 calculated for		Found			
		II	V	VI	VII
1 CH_3:	1.85		1.73	1.71	1.80
1 N:	1.73	1.78			

Lecithin.—The original alcohol-ether filtrate from which the kephalin has been removed by filtration is evaporated to dryness, and the residue dissolved in ether and freed from cholesterin by precipitation with acetone. The precipitated lecithin is treated with a large quantity of cold alcohol for some time, and the solution filtered and evaporated. The resulting lecithin should dissolve readily and completely in cold alcohol or ether. If this is not the case, the extraction with cold alcohol must be repeated. Finally, the lecithin is dissolved in hot acetic ether and allowed to separate out by cooling, dried over sulphuric acid, and analyzed.

I. 0.2420 g. of the substance gave 0.5683 g. CO_2 and 0.2420 g. H_2O; *i. e.*, 64.04 per cent. C.; 10.4 H.

II. 0.942 g. of the substance neutralized 12.1 c.c. $\frac{n}{10}$ acid; *i. e.*, 1.8 per cent N.

III. 0.677 g. of the substance gave 0.0919 g. $Mg_2P_2O_7$; *i. e.*, 3.79 per cent. P.

IV. 0.815 g. of the substance gave 0.1109 g. $Mg_2P_2O_7$; *i. e.*, 3.80 per cent. P.

V. 0.3975 g. of the substance gave 0.3156 g. AgI; *i. e.*, 5.1 per cent. CH_3.

VI. 0.235 g. of the substance gave 0.1853 g. AgI; *i. e.*, 5.03 per cent. CH_3.

My lecithin agrees fairly well in its properties with the one isolated by Thudichum (p. 116). The results of the methyl-group determination show as good an agreement with the theory as can be expected from a compound so difficult to purify.

Phosphorus as 3.8 calculated for		Found		
		III	V	VI
3 CH_3:	5.51		5.1	5.03
1 N:	1.72	1.8		

[15] *Op. cit.*, p. 130.

Lecithans from yeast.—Twenty yeast cakes are mixed well with one liter of alcohol in a flask and boiled for eight hours, filtered, the yeast allowed to stand with ether over night, filtered, the filtrates united and evaporated. The residue is extracted with cold ether, three times the volume of acetone added, and the resulting precipitate dried *in vacuo* over sulphuric acid, as it is not sufficient for further purification. The substance thus obtained resembles kephalin in that it darkens rapidly on exposure to the air and is precipitated from ether solution by alcohol. The analysis gave the following result:

I. 0.220 g. of the substance gave 0.0286 g. $Mg_2P_2O_7$; *i. e.*, 3.63 per cent. P.

II. 0.165 g. of the substance gave 0.0626 g. AgI; *i. e.*, 2.42 per cent. CH_3.

The methyl iodide was split up mostly at 240° C., but some more was obtained on raising the temperature to 300° C.

	Phosphorus as 3.63 calculated for	Found II
1 CH_3:	1.76	2.42
2 CH_3:	3.51	

The amount of methyl is not sufficient to account for two groups, and as the compound was not especially freed from lecithin, it seems reasonable to account for the extra methyl as due to an impurity of lecithin which would amount to about 11 per cent. The main bulk of the body is, therefore, kephalin, which agrees well with the other observations.

The results so far obtained with the Herzig and Meyer methyl group determine, then, that the two principal classes of lecithans differ, not only in the fatty acid group, but also in the complex which contains the nitrogen. Very striking is the fact that kephalin occurs only in living cells, such as the nerve or yeast cell, and is not found in the egg, which consists mostly of stored food material. Kephalin may possibly be an intermediary product in the decomposition of lecithin. The low amount of carbon and the correspondingly large amount of oxygen would indicate an addition of oxygen in the oleic-acid radical of the lecithin—a hypothesis which leaves unexplained the fact that kephalin is, if anything, more unsaturated than lecithin, judging by the relative amounts of iodine absorbed. At any rate, there is at present not enough known about the nature of kephalinic acid to trace its origin to oleic acid. As far as the nitrogen complex is concerned, it is possible that two methyl groups have been split off, leaving a mono-methyl oxæthylamin. Thudichum[16] has, indeed, isolated from his kephalin a base which contains less methyl groups, but he has also mentioned the presence of neurin. My results, however, show conclusively that neurin can be present only as an impurity. The decomposition of twenty grams of kephalin with barium hydrate yielded only 0.2 g. of a platinum salt, which corresponded, on analysis, to something between a mono- or a di-methyl oxæthylamin. The investigation of this interesting relation will be continued, and the methyl-group determination described above will undoubtedly be of value in following out the quantitative relation of lecithin to kephalin under various

[16] *Op. cit.*, p. 147.

conditions in the living cell. The other lecithans, such as the myelins, paramyelins, and amidomyelins, isolated by Thudichum from brain tissues, do not seem to occur in any large quantity and have not as yet been investigated.

PHYSIOLOGICAL PROPERTIES

Substances of such importance to the cell as the lecithans must possess some value as foods. The action of the digestive ferments is therefore of especial importance, as neurin, which is formed by the decomposition, has been shown by Halliburton[17] to have a decided effect on blood pressure. A. Bókay,[18] under the direction of Hoppe Seyler, investigated this problem and found that lipase will split egg lecithin into glycerophosphoric acid, fatty acids, and neurin. The three splitting products must, however, be immediately absorbed and resynthesized, as they are not found in the urine or fæces, and a meal containing considerable lecithin has never been known to cause any bad effects. The results on the metabolism of the injection of lecithin into the circulation are as yet in too unsatisfactory a state to be discussed. The patenting[19] of brain preparations for medical purposes seems, therefore, especially premature.

For completeness' sake a number of facts have been mentioned in this paper which have been known for a long time. The new facts are as follows:

1. The word "lecithan" is to be used as a group name, including such compounds as egg lecithin, brain lecithin, kephalin, myelin, paramyelin, etc.

2. The emulsion formed by the lecithans may be the substratum in which the reactions of the cell take place. The precipitation of this emulsion by divalent kations is prevented by univalent and trivalent kations, as far as investigated, and this observation may furnish an explanation of the changes brought about by electrolytes in the living cell.

3. Kephalin is found only in the living cell, and may be an intermediary product in the metabolism of lecithin.

4. An accurate method for determining lecithin and kephalin quantitatively.

[17] *Op. cit.*, p. 55.

[18] A. BÓKAY, *Hoppe Seyler's Zeitschrift für physiologische Chemie* (1877), Vol. I, p. 157.

[19] C. ZERBE, *Chemiker-Zeitung* (1902), Vol. XXVI, p. 17; Deutsches Reichs-Patent, 127357.